CLAIMS

We claim:

1. A silk-fiber-based matrix having a wire-rope geometry for use in producing a predetermined type of ligament or tendon *ex vivo*.

2. The matrix as recited in claim 1, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

3. The matrix as recited in claim 2, wherein the silk-fiber based matrix comprises fibroin obtained from *Bombyx mori* silkworm fibers.

4. The matrix as recited in claim 1, wherein the matrix comprises a composite of silk and collagen fibers.

5. The matrix as recited in claim 1, wherein the matrix comprises a composite of silk and silk fibroin fibers and one or more silk foams, films, meshes or sponges.

6. The matrix as recited in claim 1, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

7. The matrix as recited in claim 1, wherein the matrix comprise a composite of silk and one or more nondegradable polymers selected from the group consisting of

Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

8. The matrix as recited in claim 1, further comprising pluripotent or fibroblast cells seeded on said matrix.

9. The matrix as recited in claim 9, wherein said pluripotent or fibroblast cells are autologous.

10. The matrix as recited in claim 9, wherein said pluripotent or fibroblast cells are allogenic.

11. The matrix as recited in claim 9, wherein said pluripotent cells are selected from the group consisting of bone marrow stromal cells and adult or embryonic stem cells

12. The matrix as recited in claim 9, wherein said fibroblast cells are mature human ACL fibroblast cells.

13. The matrix as recited in claim 9, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said predetermined ligament or tendon.

14. The matrix as recited in claim 9, further comprising a surface modification agent which enhances poliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

15. The matrix as recited in claim 1, wherein said ligament or tendon produced is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor

tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

16. The matrix as recited in claim 15, wherein said ligament produced is an anterior cruciate ligament.

17. A silk-fiber-based matrix having a wire-rope geometry for use in producing a predetermined ligament or tendon *ex vivo*, comprising pluripotent or fibroblast cells seeded on said matrix.

18. The matrix as recited in claim 17, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

19. The matrix as recited in claim 18, wherein the silk-fiber based matrix comprises fibroin obtained from *Bombyx mori* silkworm fibers.

20. The matrix as recited in claim 17, wherein the matrix comprises a composite of silk and collagen fibers.

21. The matrix as recited in claim 17, wherein the matrix comprises a composite of silk and silk fibroin fibers and one or more silk foams, films, meshes or sponges.

22. The matrix as recited in claim 17, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

23. The matrix as recited in claim 17, wherein the matrix comprise a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

24. The matrix as recited in claim 17, wherein said pluripotent or fibroblast cells are autologous.

25. The matrix as recited in claim 17, wherein said pluripotent or fibroblast cells are allogenic.

26. The matrix as recited in claim 17, wherein said pluripotent cells are selected from the group consisting of bone marrow stromal cells and adult or embryonic stem cells

27. The matrix as recited in claim 17, wherein said fibroblast cells are mature human ACL fibroblast cells.

28. The matrix as recited in claim 17, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said predetermined ligament or tendon.

29. The matrix as recited in claim 17, further comprising a surface modification agent which enhances poliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

30. The matrix as recited in claim 17, wherein said matrix seeded with said pluripotent or fibroblast cells is cultured in vitro in a bioreactor.

31. The matrix as recited in claim 15, wherein said ligament or tendon produced is

selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

32. The matrix as recited in claim 31, wherein said ligament produced is an anterior cruciate ligament.

33. A silk-fiber-based matrix having a wire-rope geometry for use in producing a predetermined type of ligament or tendon *ex vivo*, comprising pluripotent or fibroblast cells seeded on said matrix and cultured *in vitro* in a static environment within a bioreactor.

34. The matrix as recited in claim 33, wherein said bioreactor provides conditions appropriate for cell growth and regeneration.

35. The matrix as recited in claim 33, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

36. The matrix as recited in claim 35, wherein the silk-fiber based matrix comprises fibroin obtained from *Bombyx mori* silkworm fibers.

37. The matrix as recited in claim 33, wherein the matrix comprises a composite of silk and collagen fibers.

38. The matrix as recited in claim 33, wherein the matrix comprises a composite of

silk and silk fibroin fibers and one or more silk foams, films, meshes or sponges.

39. The matrix as recited in claim 33, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

40. The matrix as recited in claim 33, wherein the matrix comprise a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

41. The matrix as recited in claim 33, wherein said pluripotent or fibroblast cells are autologous.

42. The matrix as recited in claim 33, wherein said pluripotent or fibroblast cells are allogenic.

43. The matrix as recited in claim 33, wherein said pluripotent cells are selected from the group consisting of bone marrow stromal cells and adult or embryonic stem cells

44. The matrix as recited in claim 33, wherein said fibroblast cells are mature human ACL fibroblast cells.

45. The matrix as recited in claim 33, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said predetermined ligament or tendon.

46. The matrix as recited in claim 33, further comprising a surface modification agent

which enhances proliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

47. The matrix as recited in claim 33, wherein said ligament or tendon produced is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

48. The matrix as recited in claim 47, wherein said ligament produced is an anterior cruciate ligament.

49. A silk-fiber based matrix having a wire-rope geometry for use in producing a predetermined ligament or tissue *ex vivo*, comprising pluripotent or fibroblast cells seeded on said matrix and cultured *in vitro* within a bioreactor.

50. The matrix as recited in claim 49, wherein said said bioreactor provides conditions appropriate for cell growth and regeneration.

51. The matrix as recited in claim 50, wherein said matrix is subjected to one or more mechanical signals provided by said bioreactor.

52. The matrix as recited in claim 51, wherein said mechanical signals include the application of cyclic translational and rotation strain.

53. The matrix as recited in claim 52, wherein the magnitude, duration and combination of said mechanical signals are changed over the period of culture to approach that which is experienced by a native ligament or tendon *in vivo*.

54. The matrix as recited in claim 51, wherein said mechanical signals mimic

mechanical stimuli experienced by a native ligament or tendon *in vivo*.

55. The matrix as recited in claim 49, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

56. The matrix as recited in claim 55, wherein the silk-fiber based matrix comprises fibroin obtained from *Bombyx mori* silkworm fibers.

57. The matrix as recited in claim 49, wherein the matrix comprises a composite of silk and collagen fibers.

58. The matrix as recited in claim 49, wherein the matrix comprises a composite of silk and silk fibroin fibers and one or more silk foams, films, meshes or sponges.

59. The matrix as recited in claim 49, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

60. The matrix as recited in claim 49, wherein the matrix comprise a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

61. The matrix as recited in claim 49, wherein said pluripotent or fibroblast cells are autologous.

62. The matrix as recited in claim 49, wherein said pluripotent or fibroblast cells are allogenic.

63. The matrix as recited in claim 49, wherein said pluripotent cells are selected from the group consisting of bone marrow stromal cells and adult or embryonic stem cells

64. The matrix as recited in claim 49, wherein said fibroblast cells are mature human ACL fibroblast cells.

65. The matrix as recited in claim 49, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said predetermined ligament or tendon.

66. The matrix as recited in claim 49, further comprising a surface modification agent which enhances poliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

67. The matrix as recited in claim 49, wherein said ligament or tendon produced is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

68. The matrix as recited in claim 67, wherein said ligament produced is an anterior cruciate ligament.

69. A silk-fiber based matrix having a wire-rope geometry for use in producing a predetermined ligament or tissue for implantation *in vivo* in a subject in need of a

particular ligament or tendon, said matrix being seeded with autologous cells from said subject and exposed to dynamic mechanical signals from said subject.

70. The matrix as recited in claim 69, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

71. The matrix as recited in claim 70, wherein the silk-fiber based matrix comprises fibroin obtained from *Bombyx mori* silkworm fibers.

72. The matrix as recited in claim 69, wherein the matrix comprises a composite of silk and collagen fibers.

73. The matrix as recited in claim 69, wherein the matrix comprises a composite of silk and silk fibroin fibers and one or more silk foams, films, meshes or sponges.

74. The matrix as recited in claim 69, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

75. The matrix as recited in claim 69, wherein the matrix comprise a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes.

76. The matrix as recited in claim 69, wherein said autologous cells are pluripotent or

fibroblast cells.

77. The matrix as recited in claim 76, wherein said fibroblast cells are mature human anterior cruciate ligament fibroblast cells.

78. The matrix as recited in claim 76, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said desired ligament or tendon.

79. The matrix as recited in claim 78, wherein said ligament or tendon produced is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, and lateral ligament of the ankle.

80. The matrix as receited in claim 79, wherein said ligament produced is an anterior cruciate ligament.

81. A method for producing a predetermined type of ligament or tendon *ex vivo*, comprising the steps of:

(a) seeding pluripotent or fibroblast cells within or upon a silk-fiber based matrix of cylindrical form, either pre- or post-matrix formation, to uniformly immobilize said cells within the matrix;

(b) attaching a first and a second anchor to opposite ends of said seeded matrix; and

(c) culturing said cells in the anchored matrix of step (b) under conditions appropriate for cell growth and regeneration.

82. The method as recited in claim 81, wherein said matrix comprises fibers having a wire-rope geometry.

83. The method as recited in claim 81, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

84. The method as recited in claim 83, wherein the silk-fiber based matrix comprises fibroin obtained from *Bombyx mori* silkworm fibers.

85. The method as recited in claim 81, wherein the matrix comprises a composite of silk and collagen fibers.

86. The method as recited in claim 81, wherein the matrix comprises a composite of silk and silk fibroin fibers and one or more silk foams, films, meshes or sponges.

87. The method as recited in claim 81, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

88. The method as recited in claim 81, wherein the matrix comprise a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

89. The method as recited in claim 81, wherein said pluripotent or fibroblast cells are autologous.

90. The method as recited in claim 81, wherein said pluripotent or fibroblast cells are

allogenic.

91. The method as recited in claim 81, wherein said pluripotent cells are selected from the group consisting of bone marrow stromal cells and adult or embryonic stem cells

92. The method as recited in claim 81, wherein said fibroblast cells are mature human ACL fibroblast cells.

93. The method as recited in claim 81, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said anterior cruciate ligament.

94. The method as recited in claim 81, further comprising a surface modification agent which enhances proliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

95. The method as recited in claim 81, wherein said anchors are comprised of materials selected from the group consisting of hydroxyappatite, demineralized bone, titanium, stainless steel, high density polyethylene, Dacron and Teflon.

96. The method as recited in claim 81, wherein step (c) further comprises the step of subjecting said matrix to one or more mechanical forces via movement of one or both of said first and second anchors.

97. The method as recited in claim 96, wherein said mechanical forces include the application of cyclic translational and rotation strain, said forces being independently but concurrently applied to said first anchor with respect to said second anchor.

98. The method as recited in claim 96, wherein the magnitude, duration and

combination of said mechanical forces are changed over the period of culture to approach that which is experienced by a native ligament or tendon *in vivo*.

99. The method as recited in claim 96, wherein said seeded matrix attached to said first anchor and said second anchor in step (b) is further cultured under conditions which mimic chemical stimuli experienced by said predetermined ligament or tendon *in vivo*.

100. The method as recited in claim 96, wherein said matrix is cultured and subjected to said mechanical forces within a bioreactor.

101. The method as recited in claim 96, wherein a combination of said mechanical forces are applied which simulate a combination of flexion and extension, the combination of mechanical forces being applied over time to produce said predetermined ligament or tendon having helically organized fibers.

102. The method as recited in 81, wherein said ligament or tendon produced is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

103. The method as recited in claim 102, wherein said ligament or tendon produced is an anterior cruciate ligament.

104. The method as recited in claim 96, wherein the mechanical forces mimic mechanical stimuli experienced by an anterior cruciate ligament *in vivo*.

105. A method for producing a predetermined type of ligament or tendon *ex vivo*, comprising the steps of:

(a) seeding pluripotent or fibroblast cells within or upon a silk-fiber based matrix of cylindrical form, either pre- or post-matrix formation, to uniformly immobilize said cells within the matrix;

(b) attaching a first and a second anchor to opposite ends of said seeded matrix;

(c) culturing said cells in the anchored matrix of step (b) under conditions appropriate for cell growth and regeneration, while subjecting said matrix to one or more mechanical forces via movement of one or both of said first and second anchors.

106. The method as recited in claim 105, wherein said matrix comprises fibers having a wire-rope geometry.

107. The method as recited in claim 105, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

108. The method as recited in claim 107, wherein the silk-fiber based matrix comprises fibroin obtained from *Bombyx mori* silkworm fibers.

109. The method as recited in claim 105, wherein the matrix comprises a composite of silk and collagen fibers.

110. The method as recited in claim 105, wherein the matrix comprises a composite of silk and silk fibroin fibers and one or more silk foams, films, meshes or sponges.

111. The method as recited in claim 105, wherein the matrix comprises a composite of

silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

112. The method as recited in claim 105, wherein the matrix comprises a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

113. The method as recited in claim 105, wherein said pluripotent or fibroblast cells are autologous.

114. The method as recited in claim 105, wherein said pluripotent or fibroblast cells are allogenic.

115. The method as recited in claim 105, wherein said pluripotent cells are selected from the group consisting of bone marrow stromal cells and adult or embryonic stem cells

116. The method as recited in claim 105, wherein said fibroblast cells are mature human ACL fibroblast cells.

117. The method as recited in claim 105, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said predetermined ligament or tendon.

118. The method as recited in claim 105, further comprising a surface modification agent which enhances proliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

119. The method as recited in claim 105, wherein said anchors are comprised of materials selected from the group consisting of hydroxyappatite, demineralized bone, titanium, stainless steel, high density polyethylene, Dacron and Teflon.

120. The method as recited in claim 105, wherein said mechanical forces include the application of cyclic translational and rotation strain, said forces being independently but concurrently applied said first anchor with respect to said second anchor.

121. The method as recited in claim 105, wherein the magnitude, duration and combination of said mechanical forces are changed over the period of culture to approach that which is experienced by a native ligament or tendon *in vivo*.

122. The method as recited in claim 105, wherein said seeded matrix attached to said first anchor and said second anchor in step (b) is further cultured under conditions which mimic chemical stimuli experienced by a native ligament or tendon *in vivo*.

123. The method as recited in claim 105, wherein said matrix is cultured and subjected to said mechanical forces within a bioreactor.

124. The method as recited in claim 105, wherein a combination of said mechanical forces are applied which simulate a combination of flexion and extension, the combination of mechanical forces being applied over time to produce said predetermined ligament or tendon having helically organized fibers.

125. The method as recited in claim 105, wherein said ligament or tendon produced is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

126. The method as recited in claim 125, wherein said ligament produced is an anterior cruciate ligament.

127. The method as recited in claim 105, wherein the mechanical forces mimic mechanical stimuli experienced by said predetermined ligament or tendon *in vivo*.

128. A bioengineered tissue, comprising a silk-fiber-based matrix having a wire-rope geometry and seeded with pluripotent or fibroblast cells, said pluripotent or fibroblast cells which proliferate and differentiate on said matrix to produce a predetermined ligament or tendon *ex vivo*.

129. The bioengineered tissue as recited in claim 128, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

130. The bioengineered tissue as recited in claim 128, wherein the matrix comprises a composite of silk and collagen fibers.

131. The bioengineered tissue as recited in claim 128, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

132. The bioengineered tissue as recited in claim 128, wherein the matrix comprises a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate,

Polyethylene oxide and Polyurethanes.

133. The bioengineered tissue as recited in claim 128, wherein said pluripotent or fibroblast cells are autologous or allogenic.

134. The bioengineered tissue as recited in claim 128, further comprising a surface modification agent which enhances proliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

135. The bioengineered tissue as recited in claims 128, wherein said autologous or allogenic cells form an allograft or autograft, said allograft or autograft which differentiates to form said ligament or tendon for implantation into a recipient in need thereof.

136. The bioengineered tissue as recited in claim 128, wherein said ligament or tendon produced is selected from the group consisting of ACL, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

137. The bioengineered tissue as recited in claim 136, wherein said ligament or tendon produced is an anterior cruciate ligament.

138. A bioengineered tissue produced by a method comprising the steps of:

(a) seeding pluripotent or fibroblast cells within or upon a silk-fiber based matrix of cylindrical form, either pre- or post-matrix formation, to uniformly immobilize said cells within the matrix;

(b) attaching a first and second anchor to opposite ends of said matrix;

(c) culturing said cells in the anchored matrix of step (b) under conditions appropriate for cell growth and regeneration.

139. The bioengineered tissue as recited in claim 138, wherein said matrix comprises fibers having a wire-rope geometry.

140. The bioengineered tissue as recited in claim 138, wherein said silk-fiber-based matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

141. The bioengineered tissue as recited in claim 138, wherein the matrix comprises a composite of silk and collagen fibers.

142. The bioengineered tissue as recited in claim 138, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

143. The bioengineered tissue as recited in claim 138, wherein the matrix comprise a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

144. The bioengineered tissue as recited in claim 138, wherein said pluripotent or fibroblast cells are autologous or allogenic.

145. The bioengineered tissue as recited in claim 138, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form said tissue.

146. The bioengineered tissue as recited in claim 138, further comprising a surface modification agent which enhances proliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

147. The bioengineered tissue as recited in claim 138, wherein step (c) further comprises the step of subjecting said matrix to one or more mechanical forces via movement of one or both of said first and second anchors.

148. The bioengineered tissue as recited in claim 147, wherein said mechanical forces include the application of cyclic translational and rotation strain, said forces being independently but concurrently applied said first anchor with respect to said second anchor.

149. The bioengineered tissue as recited in claim 147, wherein the magnitude, duration and combination of said mechanical forces are changed over the period of culture to approach that which is experienced by a native tissue *in vivo*.

150. The bioengineered tissue as recited in claim 147, wherein the mechanical forces mimic mechanical stimuli experienced by a native tissue *in vivo*.

151. The bioengineered tissue as recited in claim 147, wherein said seeded matrix attached to said first anchor and said second anchor in step (b) is further cultured under conditions which mimic chemical stimuli experienced by a native tissue *in vivo*.

152. The bioengineered tissue as recited in claim 147, wherein said matrix is cultured and subjected to said mechanical forces within a bioreactor.

153. The bioengineered tissue as recited in claim 147, wherein a combination of said mechanical forces are applied which simulate a combination of flexion and

extension, the combination of mechanical forces being applied over time to produce a tissue which has helically organized fibers.

154. The bioengineered tissue as recited in claim 138, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix form a desired ligament or tendon.

155. The bioengineered ligament as recited in claim 154, wherein said ligament or tendon is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

156. The bioenginnered ligament as recited in claim 155, wherein said ligament produced is an anterior cruciate ligament.

157. A bioengineered tissue produced by a method comprising the steps of:

(a) seeding pluripotent cells within or upon a silk-fiber based matrix of cylindrical form, either pre- or post-matrix formation, to uniformly immobilize said cells within the matrix;

(b) attaching a first and second anchor to opposite ends of said matrix;

(c) culturing said cells in the anchored matrix of step (b) under conditions appropriate for cell growth and regeneration, while subjecting said matrix to one or more mechanical forces via movement of one or both of said first and second anchors.

158. The bioengineered tissue as recited in claim 157, wherein said matrix comprises fibers having a wire-rope geometry.

159. The bioengineered tissue as recited in claim 157, wherein said silk-fiber-based

matrix is comprised of silk fibroin selected from the group consisting of silks from silkworms, silks from spiders, silks from genetically engineered cells, transgenic plants and animals, silks from cultured cells, native silk, silk from cloned full or partial sequences of native silk genes, and silk from synthetic genes encoding silk or silk-like sequences.

160. The bioengineered tissue as recited in claim 157, wherein the matrix comprises a composite of silk and collagen fibers.

161. The bioengineered tissue as recited in claim 157, wherein the matrix comprises a composite of silk and one or more degradable polymers selected from the group consisting of Collagens, Polylactic acid or its copolymers, Polyglycolic acid or its copolymers, Polyanhydrides, Elastin, Glycosamino glycans, and Polysaccharides.

162. The bioengineered tissue as recited in claim 157, wherein the matrix comprises a composite of silk and one or more nondegradable polymers selected from the group consisting of Polyethylene, Polystyrene, Polymethylmethacrylate, Polyethylene oxide and Polyurethanes

163. The bioengineered tissue as recited in claim 157, wherein said pluripotent or fibroblast cells are autologous or allogenic.

164. The bioengineered tissue as recited in claim 157, wherein said pluripotent or fibroblast cells proliferate and differentiate on said matrix to form a desired ligament or tendon.

165. The bioengineered tissue as recited in claim 157, further comprising a surface modification agent which enhances proliferation and differentiation of said pluripotent or fibroblast cells on said matrix.

166. The bioengineered method as recited in claim 157, wherein said mechanical forces include the application of cyclic translational and rotation strain, said forces being independently but concurrently applied said first anchor with respect to said second anchor.

167. The bioengineered tissue as recited in claim 157, wherein the magnitude, duration and combination of said mechanical forces are changed over the period of culture to approach that which is experienced by a native tissue *in vivo*.

168. The bioengineered tissue as recited in claim 157, wherein the mechanical forces mimic mechanical stimuli experienced by a native tissue *in vivo*.

169. The bioengineered tissue as recited in claim 157, wherein said seeded matrix attached to said first anchor and said second anchor in step (b) is further cultured under conditions which mimic chemical stimuli experienced by a native tissue *in vivo*.

170. The bioengineered tissue as recited in claim 157, wherein said matrix is cultured and subjected to said mechanical forces within a bioreactor.

171. The bioengineered tissue as recited in claim 157, wherein a combination of said mechanical forces are applied which simulate a combination of flexion and extension, the combination of mechanical forces being applied over time to produce a tissue which has helically organized fibers.

172. The bioengineered ligament as recited in claim 164, wherein said ligament or tendon is selected from the group consisting of anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendon, medial collateral ligament of the elbow, flexor tendon of the hand, ligaments and tendons of the temporomandibular joint, and lateral ligament of the ankle.

173. The bioenginnered ligament as recited in claim 172, wherein said ligament produced is an anterior cruciate ligament.

174. A silk-fiber-based matrix having a wire-rope geometry and seeded with bone marrow stromal cellswhich proliferate and differentiate on said matrix to produce an anterior cruciate ligament *ex vivo*.